Product Approval Information - Licensing Action

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Rockville, MD 20852-1448

April 27, 2005

Our STN: BL 125105/0

Baxter HealthCare Corporation
Baxter BioScience
Attention: Ms. Angela Blackshere
Director, Regulatory Affairs
One Baxter Way
Westlake Village, CA 91362

Dear Ms. Blackshere:

We have approved your biologics license application for Immune Globulin Intravenous (Human), 10% Solution effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Immune Globulin Intravenous (Human), 10% Solution under your existing Department of Health and Human Services U.S. License No. 140. Immune Globulin Intravenous (Human), 10% Solution is indicated for primary immune deficiency.

Under this authorization, you are approved to manufacture Immune Globulin Intravenous (Human), 10% Solution at your facility in Lessines, Belgium. You may label your product with the proprietary name GAMMAGARD LIQUID and will market it in 10 mL, 25 mL, 50 mL, 100 mL, and 200 mL fill sizes.

The dating period for Immune Globulin Intravenous (Human), 10% Solution shall be 36 months from the date of manufacture when stored at 2-8^{o}C, or not more than 9 months storage at 25^{o}C after not more than 15 months storage at 2-8^{o}C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. Following the final sterile filtration, no reprocessing/reworking is allowed withou prior approval from the Agency. Your drug substance may not be held prior to drug product formulation.

Please submit final container samples of the product in final containers together with protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologic Evaluation and Research (CBER).

You must submit information to your biologics license application for our review and written approval under 21 CFR 601.12 for any changes in the manufacturing, testing, packaging or labeling of Immune Globulin Intravenous (Human), 10% Solution, or in the manufacturing facilities.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We have reviewed your submission and agree that a deferral of your pediatric studies for Immune Globulin Intravenous (Human), 10% Solution is justified because of limited enrollment of pediatric subjects in your clinical study.

We acknowledge your written commitment as described in your letters of April 21, 2005 and April 22, 2005 as outlined below:

Postmarketing Studies subject to reporting requirements of 21 CFR 601.70.

1. Baxter has committed to providing a pediatric plan within sixty (60) days of obtaining licensure.

   Deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 601.70. These commitments are listed below.

   a. Deferred pediatric studies under PREA for the treatment of primary immune deficiency in pediatric patients.

   b. Final Report Submission: May 1, 2009.

      Submit final study reports to this BLA. For administrative purposes, all submissions related to these pediatric postmarketing study commitments must be clearly designated “Required Pediatric Study Commitments”.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 125105/0. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your BLA, STN BL 125105/0. Please use the following designators to label prominently all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Study Protocol**
- **Postmarketing Study Final Report**
- **Postmarketing Study Correspondence**
- **Annual Report on Postmarketing Studies**

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. The status report for each study should include:

- information to identify and describe the postmarketing commitment,
- the original schedule for the commitment,
- the status of the commitment (i.e. pending, ongoing, delayed, terminated, or submitted), and
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e. number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our Web site (http://www.fda.gov/cder/pmc/default.htm). Please refer to the April 2001 Draft Guidance for Industry: Reports on the Status of Postmarketing Studies – Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997 (see http://www.fda.gov/cber/gdlns/post040401.htm) for further information.

In addition, we acknowledge your written commitments of April 12, 2005 and April 18, 2005 that include the following:

Postmarketing Studies not subject to reporting requirements of 21 CFR 601.70.

In addition, pursuant to 21 CFR 600.80(c)(2)(Periodic Adverse Experience Reports), the Agency is requiring that manufacturers report on a monthly basis any infectious disease transmission associated or possibly associated with any licensed biological product that is not reportable under 21 CFR 600.80 (c)(1)(Fifteen-day Alert Reports). The timing of this monthly periodic reporting requirement was selected, among other reasons, to permit the acquisition of patient information, including clinical evaluation, sufficient to help in the timely assessment of a causal connection between the biological product and possible or documented infectious disease transmission. This new reporting requirement was also based on the observation of inconsistent practices by some manufacturers in submitting reports of possible infectious diseases.

Please note that this monthly reporting requirement applies only to infectious disease transmission. Other periodic reports should continue to be submitted on the quarterly or annual basis that is appropriate to each licensed biological product for all other adverse experiences not reportable under 21 CFR 600.80(c)(1). You should submit these monthly reports to The Center for Biologics Evaluation and Research, Division of Epidemiology, HFM-210, 1401 Rockville Pike, Rockville, MD, 20852-1448. Please contact the Division of Epidemiology (301-827-3974) if you have any questions about these periodic adverse event reporting requirements.

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and you must submit distribution reports under 21 CFR 600.81. You should submit postmarketing adverse experience reports and distribution reports to the Center for Biologics Evaluation and Research, HFM-210, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448. Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit reports of biological product deviations under 21 CFR 600.14. You promptly should identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA-3486 to the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, HFM-600, 1401 Rockville Pike, Rockville, MD 20852-1448.

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 356h and FDA Form 2567 as appropriate. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to submit two draf copies of the proposed introductory advertising and promotional labeling with an FDA Form 2253 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Branch, HFM-602, 1401 Rockville Pike, Rockville, MD 20852-1448. Two copies of final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by a FDA Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have submitted data to support such claims to us and had them approved.

Sincerely yours,

--- signature ---

Basil Golding, M.D.
Director
Division of Hematology
Office of Biologics Research and Review
Center for Biologics Evaluation and Research

Updated May 9, 2005
